the pending claims as they are believed to have been amended is attached to this Amendment and Response as an appendix.

Applicants believe that it is proper for the present amendment to be entered since it places the application in condition for allowance. Alternatively, entry of this amendment is proper since it places the claims in better form for appeal, reduces issues for appeal, does not raise any new issues, and does not require further consideration or search.

Rejections under 35 U.S.C. §112

1. Claim 19 was rejected under 35 U.S.C. §112 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

First, the specification describes methods of obtaining the human homologue of SR-B1 on page 38:lines 12-27 using the sequences disclosed in the specification. These methods fully enable one of skill in the art to obtain the human homologue of SR-B1.

Furthermore, the issue of description is adequately met simply by constructively reducing the material to practice (*Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991)). The Court in *Vas-Cath Inc. v. Mahurkar* stated, "Whether the disclosure of the application relied upon reasonably conveys to the skilled artisan that the inventor had possession at the that time [i.e., when the application was filed] of the later claimed subject matter." As long as the subject matter was described in the specification as

it was claimed, the description requirement is met. Applying this standard, the human homologue as claimed in claim 19 clearly meets the description requirement.

In so far as the Examiner is relying on *Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d. 1398 (CAFC 1997) as the basis for this rejection, Applicants note that *Regents of U.C.* is not applicable since the claims and underlying specification here are not analogous to the facts there.

The Court in *Regents of U.C.* relied on the fact that the description of example 6 in the patent at issue prophetically described obtaining a cDNA sequence from the **protein** sequence of the human protein. This is completely different then the situation here, where the specification relies on the use of the homologous cDNA as a probe, not a degenerate sequence obtained by reverse translation of a protein sequence. This difference is absolutely critical because the Court in *Regents of U.C.* relied on their own precedence of *In re Deuel* 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (1995). The Court stated, "A prior art disclosure of the **amino acid sequence** of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences encoding for the protein." In relying on the relationship of amino acid sequence to nucleic acid sequence, *Regents of U.C.* is limited to protein-to-DNA situations. It should be noted that the court in *Regents of U.C.* did not specifically address (and thus, did not overrule) the standard that has

been accepted for the description requirement for the last 125 years, most recently explicated in *Vas-Cath Inc. v Mahurkar.*

2. Claims 9-13, 15, 17, 19-22, and 44-50 were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for protein sequences other than those in SEQ ID Nos. 4, 6, and 8. This rejection is respectfully traversed.

The claims are limited by the requirement that the cDNAs encoding the type B1 scavenger receptors must hybridize to the nucleic acid molecule of SEQ ID No. 2. Applicants object to the characterization that "Any nucleic acid molecule will hybridize to any other nucleic acid molecule under the appropriate conditions, irrespective of the degree of sequence similarity between the molecules being hybridized." While it is true that the specificity of nucleic acid interaction, or hybridization, can be affected by the conditions that the hybridization occurs under, those of skill in the art know how to perform hybridization experiments that lead to specific gene recognition of homologues, and the present application **specifically describes** how to do this for a SR-B1 cDNA. For example, on page 18:line 27 to page 19:line 6 an explicit description of a hybridization procedure in which the isolated hamster SR-B1 cDNA is used to produce a 600 base probe (derived from a BamHI restriction digest of the DNA shown in Seq ID No. 3) which is used to probe different cell types from murine tissues and from 3T3 cells. The hybridization and washing conditions were done at 42° C and 50° C respectively using the well known conditions described by Charron et al. *Proc. Natl. Acad. Sci.* 86 2535-2539 (1989). Performing the hybridization

analysis as described in the application clearly shows that a single predominant band of 2.4 kb was abundant in fat and present in moderate levels in lung and liver (page 31:line 11 to page 32:line 24). While the 600 base probe derived from the hamster scavenger receptor type B1 cDNA hybridizes as single gene sequence in mouse, a probe from CD36 has a different hybridization pattern, indicating that the hybridization assay described is sufficient to differentiate between CD36 and applicants' nucleic acids encoding SR-B1 type proteins. This fact is significant since, as pointed out in the Office Action, other non-SR-BI genes are closely related in sequence to hamster and human SR-BI sequence (see Calvo et al.). This indicates that while CD36 and SR-B1 are related proteins (both members of the CD36 superfamily), they are not so related as to be considered homologues with each other. The hybridization methods described in the specification clearly indicate that the scope of the claims is such that it would not include all members of the CD36 superfamily, only those that are in the class defined by the specification as type SR-B1. In other words, the hybridization recited in the claims, when read in light of the specification, results in the inclusion of SR-BI encoding sequences, but excludes sequences encoding non-SR-BI proteins (including other members of the CD36 superfamily).

The present rejection is based on the erroneous premise that the specification does not provide the guidance that is required to produce nucleic acids encoding proteins whose amino acid sequences have been substantially altered from natural forms in a predictable manner. The application provides numerous assays for determining the function of an SR-B1 receptor

such as binding AcLDL. Contrary to the Examiner's assertion in the Office Action mailed June 26, 1997, these assays allow those of skill in the art to determine which variants are functional and which are not functional.

As described in the application, once one nucleic acid encoding type BI scavenger receptor protein was obtained, it was routine to isolate a second molecule. As described in the application, it was routine to make and use both monoclonal and polyclonal antibodies to the type BI scavenger receptor protein.

3. Claim 49 was rejected under 35 U.S.C. §112, first paragraph, as the subject matter is allegedly not described so that one of skill in the art could make and use the invention. This rejection is respectfully traversed.

Claim 49 is drawn to a method of inhibiting uptake of lipoprotein or lipids by adipocytes comprising a method of selectively inhibiting the uptake by a scavenger receptor protein encoded by a nucleic acid which hybridizes to SEQ ID Nos. 3 and 7 and selectively binds a low density lipoprotein, modified lipoprotein, or acetylated protein under conditions wherein the low density lipoprotein is bound to the scavenger receptor.

Applicants have not "overlooked the fact that claim 49 is drawn to a method of treatment" because as Applicant reads claim 49 it is not specifically drawn to a method of treatment. It is drawn to a method of inhibiting uptake of a scavenger receptor protein of the type described in this application. In this light the remarks made by Applicant in the Response mailed on December 29, 1997, are completely responsive, contrary to the

Examiner's assertions. The application does indeed show numerous binding studies in which competitive inhibition and alteration of binding is demonstrated. Figures 3A and 3B; 4A and 4B; 5; 7A-E do relate data that indicates inhibition of binding and uptake by the Type B1 scavenger receptor. These actual working examples clearly demonstrate that such assays are routine and would require absolutely no undue experimentation. These examples demonstrate that the limitation of claim 49, "inhibition of scavenger receptor binding and uptake," is clearly enabled by the specification.

Applicants also assert that no proper *prima facie* case for lack of enablement has been established. The standard for making a rejection based on 35 U.S.C. § 112, first paragraph is articulated in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) (see also MPEP § 2164.01 and 2164.04). Initially, the Patent Office must accept the objective truth of statements made in the specification. If such statements are to be called into question, the Patent Office is burdened with providing evidence or convincing argument why those of skill in the art would doubt the statements (*In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). Applicants assert that this burden has not been met. The Office Action provides no evidence or convincing argument, as required, that the claimed method could not be used for the "method of treatment" purposes focused on by the Examiner, let alone for the minimal use required for enablement (see discussion below). Thus, no proper *prima facie* case for lack of enablement has been established. The rejection offers no support for, or explanation of, the conclusion that the results of experiments involving inhibition of binding are not predictable.

The rejection also fails to establish that such unpredictability is pertinent to the predictability of a method of inhibiting binding or uptake, or dispositive of the enablement of the claimed method. In this regard, Applicants note that the claims are not directed to, and do not require an efficacious method of treatment as asserted by the Examiner. On the contrary, the claims require only inhibition of binding of lipids by the scavenger receptors of the present application.

The fact, relied upon by the Examiner, that there are no working examples in the specification is non-sequitur. Just because the claimed method and similar methods were not demonstrated to be therapeutically efficacious is not evidence that such use is unpredictable or that such use can not be established without the need for undue experimentation, or that those of skill in the art would doubt that the claimed method could be used *in vivo*. In this regard, Applicants note that there is no requirement that the claimed method be actually demonstrated.[1/] The lack of an actual demonstration of the present method *in vivo* cannot, by itself, be dispositive of whether the method will work *in vivo* because, *inter alia*, the claimed method is as yet unknown to those of skill in the art. Accordingly, the "failure" to demonstrate the present method *in vivo* provides no evidence that any difficulty would be

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[1/]See *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987) (the mere fact that something has not previously been done is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it).

encountered in using the claimed method *in vivo*. For all of these reasons a proper *prima facie* case for lack of enablement has not been established.

Applicants note that the present rejection concerns itself only with the question of whether the specification adequately teaches those of skill in the art how to use the claimed method as a *method of treatment*. Although Applicants have provided sufficient disclosure to allow those of skill in the art to use the claimed method therapeutically (see above), Applicants are not required to do so for the specification to meet the requirement of 35 U.S.C. § 112, first paragraph. In this regard it is important to note that the claims are directed to a method for inhibiting binding and uptake of lipids and lipoprotein by the scavenger receptors of the present application, not to achieving a therapeutic result. It is axiomatic that only that which is actually claimed need be enabled.[2/] Thus, for the specification to teach how to make and use the claimed invention, all that is required is a discussion of molecules and assays that inhibit the uptake of lipids or lipoproteins by type B1 scavenger receptors. In this regard, Applicants direct attention to *In re Gardner*, 475 F.2d 1389, 1392 (CCPA 1973), *reh'g denied*, 480 F.2d 879 (CCPA 1973), where the court

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[2/]see *Christianson v. Colt Industries Operating Corp.*, 822 F.2d 1544, 1565, 1 USPQ2d 1241, 1255 (Fed. Cir. 1987), *vacated, and remanded with instructions to transfer appeal to Court of Appeals for the Seventh Circuit*, 108 S. Ct. 2166,, 7 USPQ2d 1109 (1988), *on remand*, 870 F.2d 1292, 1299, 10 USPQ2d 1352, 1357 (7th Cir. 1989) ("Because only the claimed invention receives patent law protection, the disclosures need generally be no greater than the claim.") ("The 'invention' referred to in the enablement requirement of section 112 is the *claimed* invention").

emphasized that the subject matter within a broad claim need not be shown to have the same degree of utility; it is sufficient if the specification adequately discloses some use for all of the subject matter.[3/] Applicants assert that even for the method of treatment uses at issue, Applicants are not required to support or demonstrate some arbitrary level of use or effectiveness. All that is required is that the invention work to some extent and that this minimal level of use is enabled. For example, it is not required that the claimed method cure any disease, prolong life, or even inhibit the binding of the lipoprotein molecules to the SR-B1 receptor for some specific period of time. All that is required is that the claimed method, at a minimum, inhibit the uptake of lipoprotein (or other limitations of the claim) by an SR-B1. Applicants assert that there can hardly be any question that the claimed method will accomplish this. Contrary to the implication of the rejection, the "use" of the claimed method enabled by the specification need not be a commercially viable therapeutic treatment

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[3/]See also *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762 (Fed. Cir. 1984) ("the fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility."); *Ex parte Hozumi*, 3 USPQ2d 1059, 1060-61 (Bd. Pat. App. & Int'f 1987) (as to examiner's Section 112 rejection "based on an asserted lack of enablement with respect to the utilization of the entire genus disclosed in the antitumor utility disclosed": "it is not necessary that all of the compounds claimed be useful for every utility disclosed in an application"); *Ex parte Cole*, 223 USPQ 94, 95 (PTO Bd. App. 1983) ("We know of no statutory or case law requiring each and every compound within a claim to be equally useful for each and every contemplated application.").

or even a therapeutically efficacious treatment.[4/] Applicants are not required to demonstrate a safe and effective therapeutic treatment, especially when the claims do not require such a capability.

Applicants also note that ample guidance needed for the practice of the claimed method appears on pages 43 to 54 of the specification. For example, on page 43:line 36 to page 44:line 22 the specification provides the exact element required in the rejection -- a relationship between *in vitro* data and *in vivo* use. Because of the highly conserved nature of these proteins, the pathway from *in vitro* inhibition to *in vivo* use, via animal modeling, is highly predictive and successful. Applicants also direct attention to pages 53 and 54 where methods of delivery of the inhibiting compounds and probable dosages are described. Thus, the specification cannot be seen as providing "no guidance" and clearly meets the requirements of U.S.C. 35 § 112.

[4/]see *In re Langer*, 183 USPQ 288, 298 (CCPA 1974) (full scale clinical trials in humans...may be necessary to establish 'commercial usefulness' in this technology. However, development of a product to the extent that it is commercially salable in the marketplace is not required to establish 'usefulness'); see also *Ex parte Maas*, 14 USPQ2d 1762, 9 USPQ2d 1746, 1747 (Bd. Pat. App. & Int'f 1987) (appeal presents "only one issue...whether [Applicants] have provided substantiating evidence...to establish that the subject matter defined [in the claims] possesses a practical utility"; "the issue under 35 USC 112 relating to an enabling disclosure is subsumed within the issue under 35 USC 101 relating to patentable utility"); *In re Hafner*, 410 F.2d 1403, 1405, 161 USPQ 783, 785 (CCPA 1969) ("The disclosure of how to use must relate to a use of the kind considered by the Supreme Court in Brenner v. Manson to be a sufficient utility.").

4. Claims 44-50 were rejected under 35 U.S.C. §112, first paragraph, for allegedly being incomplete. These rejections are respectfully traversed.

The claimed methods in conjunction with the specification are absolutely clear and complete. One of skill in the art would be able to practice, without undue experimentation, the claimed methods. For example, the Examiner has singled out the recitation of "providing reagents for use in an assay for binding" in claim 44, as incomplete. The specification provides numerous examples of reagents for binding, such as AcLDL and M-BSA to name two. The Examiner is directed to page 28:line 15 to page 31:line 10 where there is extensive description of binding assays and binding reagents. Claims 44-50 are complete in their recitation of the necessary steps which set out the claimed methods. As outlined in *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971), the breadth of a claim is not to be equated with indefiniteness. The MPEP (2173.04) states, "If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, first paragraph would be appropriate." Claims 44-50 are clear and Applicants have not indicated that the invention covers something other than that defined by the claims, therefore, APplicants respectfully traverse the above rejection.

Rejections Under 35 U.S.C. § 112, second paragraph

1. Claims 9-15, 19-22, and 44-50 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite as to the term "scavenger receptor protein type BI". These rejections are respectfully traversed.

Contrary to the Examiner's assertion that "The two elements 'encoding a protein X' and 'which hybridizes to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO:## under stringent hybridization conditions' are two properties of a nucleic acid molecule which are not mutually inclusive nor is one a subset of the other," Applicants assert that these properties do, in conjunction with the other limitations of the claims, distinctly claim the subject matter. It is axiomatic that nucleic acids define the proteins for which they encode. Furthermore, as the specification abundantly indicates, the nucleic acid of SEQ ID Nos. 3 and 7 does specifically and accurately define the scope of the claim.

In so far as the Examiner's assertion is directed to the function of the protein, the claims also include functional limitations such as "binding lipoprotein" which when coupled with the hybridization limitation do couple the cDNA to the protein that it encodes. The compositions and methods described in the present application define a new family of cDNAs which encode for a novel type of scavenger receptor protein, termed type BI. These cDNAs are related in that they hybridize to the sequences described in SEQ ID Nos. 3 and 7, and in that they encode for a novel type of scavenger receptor having the functional properties clearly defined in the claims and in the specification as a whole.

2. Claims 9-12, 15, 19-22, and 44-50 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite because of the term "hybridizing". These rejections are respectfully traversed.

Claims are to be interpreted in light of the specification. As outlined above the term hybridizing can clearly be interpreted from the specification as a whole. It is not required that all of the conditions for a given term be recited in the claims when the specification as a whole clearly sets forth the meaning of the term.

Claim 9 was rejected under 35 U.S.C. §112, second paragraph, for not having an antecedent basis for "scavenger receptor protein type B-1." Claim 9 has been amended to refer to "a" scavenger receptor protein, as suggested by the Examiner.

Claim 14 was rejected under 35 U.S.C. §112, second paragraph, for allegedly being vague and indefinite for reciting "or a degenerate thereof." The Examiner states, "Either the claimed nucleic acid encodes the amino acid Sequence ID NO:4 or it doesn't." The degeneracy of the DNA code is well known to those of skill in the art, and is understood to mean those DNA sequences which code for a given amino acid sequence. Claim 14 is not indefinite with respect to the degeneracy that is inherent in the genetic code.

Claim 21 was rejected under 35 U.S.C. §112, second paragraph, for allegedly being vague and indefinite because of no physical relationship between the "molecule of claim 11 and the "expression vector." Claim 21 has been amended to more clearly indicate that the

nucleic acid sequence of claim 11 and the nucleic acid sequence of the expression vector are connected.

Claim 22 was rejected under 35 U.S.C. §112, second paragraph, for allegedly being vague and indefinite because of no physical relationship between the "composition of claim 21" and the "host cell." Claim 22 has been amended to more clearly indicate the claimed subject matter which is a host cell suitable for expression of a scavenger receptor that comprises the nucleic acid molecule of claim 21.

Claim 46 is allegedly confusing because the term "naturally occurring or synthetic compounds" implies a third alternative. Applicants believe the Amendment filed December 29, 1997, addresses this issue. Specifically, claim 46 has been amended to refer to "compounds", rather than "naturally occurring or synthetic compounds."

Rejection under 35 U.S.C. §102

Claims 11,12,15, 17, 19 and 20 were rejected under 35 U.S.C. §102(a) as being anticipated by Calvo et al. (J. Biol. Chem. 268(25) 18929-18935 (1993)). This rejection is respectfully traversed.

Calvo, et al. reported isolation of a cDNA encoding a member of the CD36 superfamily. The protein was not physically isolated nor was the cloned DNA expressed on the surface of cells and shown to be functional, although a small piece (the carboxyl terminal region including residues 365-409) was expressed as a chimeric protein (page 18930). The function of the protein was not known, although its resemblance to CD36/LimpII was

recognized based on the predicted similarities in structure and the authors speculated that "on the basis of its structural homology to CD36 that CLA-1 could act as a receptor for extracellular products" (page 18934).

A Declaration under 37 C.F.R. §1.131, submitted in the parent application, U.S. Serial No. 08/265,428, filed June 23, 1994, which demonstrates that a cDNA and encoded protein defined by the claims in issue was reduced to practice prior to the publication of Calvo, et al. was submitted with the Response to An Office Action, mailed on December 29, 1997. Applicants cloned the gene, they expressed the protein, and they characterized the protein and showed its function, **prior to** Calvo's publication date.

37 C.F.R. § 1.131 states, in pertinent part,

> (a)(1) When any claim of an application . . . is rejected under 35 U.S.C. 102 (a) or (e), or 35 U.S.C. 103 based on . . . reference to . . . a printed publication, the inventor of the subject matter of the rejected claim . . . may submit an appropriate oath or declaration to overcome the . . . publication. The oath or declaration must include facts showing a completion of the invention in this country or in a NAFTA or WTO member country before . . . the date of the printed publication.
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> * * *
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> (b) The showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the

invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice . . . .

The Applicant need only provide evidence that reasonably gives rise to an inference that the invention was completed before the reference date, in order to constitute a prima facie showing. No corroboration is required since the application process is ex parte. A Rule 131 affidavit is sufficient when it demonstrates that the Applicant has prior "possession" of that part of the invention disclosed by the reference, as is the case when a reference discloses a species falling within a claim to its genus. *See* Donald S. Chisum, **Patents** § 3.08[1][b] (Matthew Bender & Co. 1996). Possession in this context is shown by demonstrating conception, reduction to practice, and diligence--each as normally required in determining the date of invention. *See* In re Mulder, 716 F.2d 1542 (Fed. Cir. 1983).

The Krieger and Acton Declaration clearly shows that the Applicants were in possession of the cDNA and expressed protein prior to the date of Calvo et al.

In In re Stempel, 241 F.2d 755 (C.C.P.A. 1957), the court held that Applicant's affidavit under Rule 131 was not required to show priority with respect to the claimed genus, but only to the species disclosed by the cited reference, in order to remove that reference as prior art. The claims, both genus and species were drawn to chemical compounds. Stempel overcame the anticipation rejection by showing reduction to practice, prior to the effective date of the reference, of a species of the invention within the generic claims.

In In re Tanczyn, 347 F.2d 830 (C.C.P.A. 1965), the court qualified In re Stempel, stating that the Stempel doctrine did not apply to *partial* possession of the invention, as distinguished from *total* possession of a species within a genus claim. The Tanczyn application "did not involve a genus-species relationship." Id. at 833. The court reaffirmed Stempel in its application to rejections under 35 U.S.C. § 102(a), but held in reference to § 103 rejections,

> "[w]e never intended . . . to authorize the overcoming of references by affidavits showing that the Applicant had invented, prior to the reference date, a part, some parts, or even a combination of parts, used to create an embodiment of his claimed invention, where the part or parts are not within the scope of the claims being sought, as the species of Stempel shown by the reference was within his generic claims . . .. It is not sufficient to show in a Rule 131 affidavit that an invention is wholly outside of that being claimed was made prior to the reference date. Such fact is irrelevant."

In In re Clarke, 356 F.2d 987 (C.C.P.A. 1966), the court extended the Stempel doctrine to the situation at issue in this application, that is where the Applicant's Rule 131 affidavit shows possession that is *not* of the entire invention nor of the part of the invention disclosed by the reference. The Clarke court held that the affidavit is sufficient to remove a reference where the Applicant demonstrates possession of such "invention" as to make the entire claimed invention or the reference part obvious to one of ordinary skill in the art. The court stated,

"[i]n an appropriate case an Applicant should not be prevented from obtaining a patent to an invention where a compound described in a reference would have been obvious to one of ordinary skill in the art in view of what the affiant proves was completed with respect to the invention prior to the effective date of the reference. . . . Thus, we think that in an appropriate case a single species could be sufficient to antedate indirectly a different species of a reference.".

The CCPA also has phrased the rule, "[w]hen that species of the generic invention which has been completed prior to the effective date of the reference would make obvious to one of ordinary skill in the art the species disclosed in the reference, the reference may be said to have been 'indirectly antedated.'" In re Schaub, 537 F.2d 509, 512 (C.C.P.A. 1976) (quoting In re Ranier, 390 F.2d 771, 773-74 (C.C.P.A. 1968)). The Schaub court stated that "[a]ppellants have made a prima facie case that the compound of the reference is obvious from the compounds which they have made prior to the date of the reference. Appellants' compound III is the next higher homolog of the reference compound II, . . ." Id. at 512-13.

There is little, if any, Federal Circuit case law on point. However, the rule established in In re Clarke apparently remains valid, as one somewhat recent, "unpublished" (i.e. not citable as precedent) case seems to indicate. In In re Rozmus, 928 F.2d 412, 1991 WL 17232 (Fed. Cir.), the court stated that "[a]lthough Rozmus' [Rule 131] declaration showed reduction to practice of only a species of the generic invention, that alone is not fatal to his claim. A declaration proving a species is also sufficient to show possession of

'variations and adaptations which would, at the same time, be obvious to one skilled in the art.'" (quoting In re Spiller, 500 F.2d 1170, 1178 n.5 (CCPA 1974)).

Other cases discussing priority but which do not involve Rule 131 have stated, "[p]riority as to a genus may . . . be shown by prior invention of a single species, but the genus will not be patentable to an Applicant unless he has generic support therefor." In re Zletz, 893 F.2d 319, 323 (Fed. Cir. 1989); *see also* Hoffman v. Schoenwald 15 U.S.P.Q.2d 1512, 1514 (Bd. Pat. App. & Int'f 1990) ("Conception of a species within the genus constitutes conception of the genus for priority of invention purposes.").

The Examiner has stated that the Declaration under § 1.131 does not "demonstrate that the Applicant was in possession of the any information regarding a CLA-1 protein or CLA-1 gene from any animal other than hamster prior to the publication of Calvo et al." Applicants respectfully point out that this is not in fact true. Submitted with the Declaration is a printout obtained from the search of six databases (PDP, Swissprot, PIR, SPupdate, Genpept, GPupdate). This printout indicates that the Rat LimpII gene and the CD36 gene were among the genes with the highest homology to SR-B1. While these genes have been shown to be members of a different family within the superfamily of CD36 scavenger receptors than the SR-B1 proteins of the present application, for one of ordinary skill in the art they presented a nexus between the species described in the Declaration of Krieger and Acton and the genus which would include the CLA-1 gene described in Calvo et al.

Furthermore, the Examiner has stated, "There is no evidence in this Declaration that a nucleic acid probe encoding all or part of hamster CLA-1 was capable of hybridizing to mouse DNA or that a DNA encoding a murine cDNA had been isolated." This statement is incorrect. The specification provides exactly the type of evidence the Examiner is looking for. For example, on page 18:line 27 to page 19:line 6 there is an explicit description of a hybridization procedure in which a 600 base probe of derived from the hamster SR-B1 cDNA is used to probe different cell types from murine tissues and from 3T3 cells. The results from these experiments clearly shows that a single predominant band of 2.4 kb was abundant in fat and present in moderate levels in lung and liver (page 31:line 11 to page 32:line 24). This data not only directly indicates an interspecies hybridization abundance, it indicates that this relationship is specific and successful because it recognizes the murine homologue in only those tissues that express it. The genus of the claims is described as cDNAs encoding Scavenger Receptor Protein type B1, having specific functional properties, and includes the SR-B1 cDNA of the present application and the CLA-1 cDNA of Calvo et al. This genus is a subgenus of the genus of CD36 superfamily of scavenger receptor proteins which includes CD36 and LimpII.

To one of ordinary skill in the art there would have been more than sufficient motivation given the sequence homology data presented in the Declaration to utilize the information obtained from the novel hamster SR-B1 to isolate the human homologue based

on the information provided in the specification and the general knowledge known in the art. As discussed below, this view is also held and argued by the Examiner.

Rejection under 35 U.S.C. §103

Claims 9, 10, 13, 14, 18, 19, 21 and 22 were rejected under 35 U.S.C. §103 as obvious over Calvo, et al. J. Biol. Chem. 268(25), 18929-18935 (1993). These rejections are respectfully traversed.

The Examiner has maintained the above rejection for the reasons cited in the Office Action dated March 29, 1997. Among the reasons that the Examiner has cited that it would be obvious to go from the Human CLA-1 gene described by Calvo et al. to the hamster homologue of the present application are: (1) CLA is described as being structurally analogous to LIMPII: (2) amino acid sequence were highly conserved between human and rat LIMPII were highly conserved; (3) the genes had sufficient similarity to permit the isolation of LIMPII; (4) an artisan would have concluded that any mammalian protein encoding CLA-1 would have been readily isolated by probing a DNA library, the hamster, as well as rat, was routinely employed as a laboratory model for determining the physiological significance if proteins of human origin since the scope of human experimentation is obviously limited, would have found it *prima facie* obvious to go from the human version of CLA-1 to the hamster version of CLA-1, or SR-B1; (5) and there was knowledge that there was homology between humans and rodents at the time. [Applicants note, in passing, that each and every one of these reasons, relied upon by the Examiner to support the "prima facie" case of

obviousness to clone the hamster SR-B1 protein from the sequence information of the human CLA-1 protein is present in the specification and Declaration in the present application. This supports applicants' traversal of the 102 rejection above.]

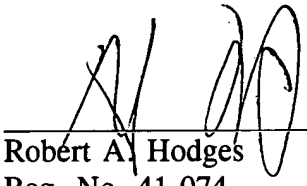
Applicants do not understand how, in the light of the Declaration submitted, the Examiner can maintain that it was prima facie obvious to clone the hamster homologue of the human CLA-1 when applicants have demonstrated possession of the hamster gene before the date of the publication of the human homologue CLA-1. Furthermore, in light of the Examiner's rejection of claim 19 under 35 U.S.C § 112 for an inadequate description of the human homologue of SR-B1, which implicitly relies on Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d. 1398 (CAFC 1997), it is inconsistent to maintain a rejection which is contrary to the Examiner's only interpretation and reliance on case law. Applicants as stated above, distinguish themselves not only from Regents of the University of California v. Eli Lilly and Company (as discussed above), but also assert that in the light of the Declaration and the evidence provided in the specification, it would have been prima facie obvious to clone the human homologue of SR-B1 which as it turns out is CLA-1.

Applicants have demonstrated that they cloned and expressed the hamster gene encoding the claimed SR-BI proteins, and that the gene hybridizes to the murine gene, prior to publication by Calvo et al. Accordingly, Applicants conceived of and reduced to practice the claimed invention prior to Calvo et al. Therefore, the Declaration under 37 C.F.R.

§1.131 should conclusively remove Calvo et al. as a reference, and the claims found patentable to Appellants.

Allowance of all claims 9-15, 19-22, and 44-50, as amended, is earnestly solicited.

Respectfully submitted,



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Date: July 20, 1998

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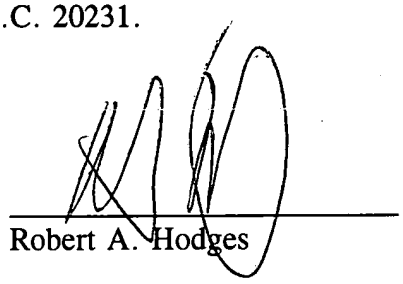

Robert A. Hodges

Date: July 20, 1998